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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,288	11/28/2000	Dale B. Schenk	15270J-004765US	9431
20350 7590 10/03/2007 TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834			EXAMINER BALLARD, KIMBERLY A	
			ART UNIT 1649	PAPER NUMBER
			MAIL DATE 10/03/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<p align="center">Office Action Summary</p>	<p>Application No.</p> <p align="center">09/724,288</p>	<p>Applicant(s)</p> <p align="center">SCHENK ET AL.</p>	
	<p>Examiner</p> <p align="center">Kimberly A. Ballard</p>	<p>Art Unit</p> <p align="center">1649</p>	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 90-94,96-98 and 100 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 90,91,93,94 and 96 is/are rejected.
- 7) ☒ Claim(s) 92,97,98 and 100 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/20/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

Claims 90, 91 and 98 have been amended as requested in the response filed July 20, 2007. Claims **90-94**, **96-98**, and **100** are pending and under examination in the current office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

A signed and initialed copy of the IDS paper submitted July 20, 2007 is enclosed in this action. The European and PCT search reports (document Nos. 852, 850 and 872) have been considered, but the individual references contained within these search reports have not been considered, nor will they be entered of record unless they are presented on an IDS in the proper format and copies of each are provided to the Office.

Withdrawn Objections and Claim Rejections

The rejection of claims 90-94, 96, 97 and 100 under 35 U.S.C. 112, first paragraph, as set forth at pp. 3-7 of the previous Office action (mailed 04/23/2007) is withdrawn in view of the claim amendments and Applicants' arguments.

The rejections of claims 90 and 91 under 35 U.S.C. 112, second paragraph, set forth at pp. 7-8 of the previous Office action (mailed 04/23/2007) is withdrawn in view of the amendments to the claims.

New Claim Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 90, 91, 93, 94 and 96 are rejected under 35 U.S.C. 102(b) as being anticipated by Ard et al. (*J. Neurosci Res.* 1996; 43:190-202; a copy of this reference can be found in parent application 09/322,289, in the IDS filed 05/07/2007).

The claims are drawn to a method of screening an antibody for activity in inducing clearance of an amyloid deposit of A β , comprising combining the deposit, the antibody, and microglial cells bearing Fc receptors in a medium in vitro and monitoring the amyloid deposits by a series of measurements (claim 90), wherein the amount of amyloid deposit remaining is assessed by the amount of an antigen associated with the amyloid deposits remaining in the medium (claim 91), wherein the antigen is A β (claim 94), wherein the amyloid deposit is a tissue sample from the brain of an Alzheimer's disease patient or an animal having Alzheimer's pathology (claim 93), and wherein the monitoring is performed microscopically (claim 96).

Ard et al. teach that cultured microglia cells have a high capacity to clear A β peptide, such as by phagocytosing and internally accumulating the protein (see abstract and Figure 1). Ard thus discloses a method of assessing the ability of microglia cells to clear A β protein, wherein the monitoring was performed by electron microscopy, thus meeting a limitation of instant claim 96, or by immunoblotting techniques to determine the amount of A β in the culture medium (see p. 193, 1st column), thus anticipating claim 91. In the experiments disclosed by Ard, cultured microglia cells were exposed to either synthetic A β protein aggregates (A β 1-42) or human brain tissue samples from Alzheimer's disease patients (see "Materials" on p. 191) either in the absence or presence of serum. The skilled artisan is well aware that serum, such as the fetal bovine serum used in these experiments, contains immunoglobulin molecules, which would therefore meet the limitation of "an antibody". The skilled artisan is also aware that microglial cells inherently bear Fc receptors on their cell surface (discussed in previous Office actions).

Ard notes that the addition of serum to the A β /microglia cultures in most circumstances decreased the ability of the microglial cells to accumulate A β (see p. 196 and Figures 6-9). The measurement of A β accumulation by microglia in serum-free medium would thus constitute a baseline measurement, to which the cultured system in the presence of serum was compared. The pre- and post-serum conditions would also meet the limitation of a "series of measurements", as there is no defining number for what constitutes a series, per se. Regardless, Ard teaches that different concentrations of A β were added to the culture medium and the ability of microglia cells to clear the A β

from the culture medium in the presence of serum was also compared (see Figure 6), which would also anticipate the "series of measurements" recited limitation. Accordingly, the experiments described by Ard et al. demonstrate a method of determining the effects of serum (i.e., an antibody) on the activity of microglial to clear A β from the culture. Although Ard does not explicitly comment on the immunoglobulin molecules contained within the serum, their presence in the serum and their effects on the microglia cells would be inherent to the cultured system. In this case, there was no reduction in the amount of amyloid deposit remaining in the medium following the addition of serum immunoglobulin molecules, indicating that these particular immunoglobulins (i.e., antibodies) do not induce phagocytic clearing activity. Finally, Ard notes that she disclosed microglia culture system which studies the clearance of A β or accumulation as aggregates allows for the investigation of other factors that may either promote or inhibit A β removal or deposition and modify the course of β -amyloidosis in Alzheimer's disease. Such teachings are further evidence that the methods disclosed by Ard et al. could be readily used to screen antibodies for activity in inducing clearance of A β deposits. Accordingly, the teachings of Ard et al. anticipate the instant invention of claims 90, 91, 93, 94 and 96.

Conclusion

Claims 90, 91, 93, 94 and 96 are rejected. Claims 92, 97, 98 and 100 are objected to as being dependent upon a rejected base claim, but would otherwise be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on Monday-Friday 9AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard, Ph.D.
September 25, 2007

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646